University of Alberta

Predicting postoperative pulmonary complications after non-thoracic surgeries: A prospective cohort study

by

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Abstract

This study was conducted to determine if elements of the history, physical examination and operative factors among participants undergoing non-thoracic surgeries can predict pulmonary complications postoperatively. Adult patients scheduled to undergo elective non-thoracic surgical procedures at the University of Alberta Hospital were approached consecutively for participation in the study. Information was collected on health histories, physical examinations, and operative factors prospectively. Investigators determining outcomes were blinded to participants' preoperative data. Postoperative pulmonary complications developed in 20 of 745 (2.68%) participants. Several variables were associated with the development of pulmonary complications after bivariate analyses. Only three variables remained significant after multivariate analysis: nasogastric tube placement perioperatively (OR 8.74), age $\geq$ 65 years (OR 8.91), and length of operation $\geq$ 2.5 hours (OR 3.13). In conclusion, preoperative and operative factors can identify patients who are at increased risk for pulmonary complications after non-thoracic surgery. Sample size limitations require caution in generalizing these findings.

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Table of Contents

Chapter 1: Introduction..... 1

1.1. Background on Postoperative Pulmonary Complications..... 1

1.2. Lack of Clinical Prediction Rules for Preoperative Evaluation of Pulmonary Risk..... 1

1.3. Methodological Features in Diagnostic Studies Which Are Important in Avoiding Bias..... 2

1.4. The Literature on Preoperative Pulmonary Risk Prediction..... 5

1.5. Summary of Preliminary Study..... 10

Chapter 2: Study Objectives and Hypothesis..... 15

2.1. Study Objectives..... 15

2.2. Hypothesis..... 15

Chapter 3: Methods..... 16

3.1. Study Design..... 16

3.2. Setting..... 16

3.3. Timeline..... 16

3.4. Data Collectors..... 16

3.5. Study Participants..... 17

3.5.1. Inclusion Criteria..... 17

3.5.2. Exclusion Criteria..... 17

3.5.3. Refusals..... 19

3.6. Consent and Data Collection Forms..... 19

3.6.1. Consent Form and Information Sheet..... 19

3.6.2. Data Collection Form..... 19

3.7. Procedures..... 20

3.7.1. History..... 20

3.7.1.1. Age..... 20

3.7.1.2. Gender..... 20

3.7.1.3. Height and Weight....21
3.7.1.4. Smoking Status....21
3.7.1.5. Recent Upper Respiratory Tract Infection....22
3.7.1.6. Self-Reported History of Chronic Obstructive Pulmonary Disease....22
3.7.1.7. Self-Reported History of Asthma....22
3.7.1.8. History of a Daily Cough....23
3.7.1.9. Exercise Capacity....23
3.7.2. Physical Examination....23
3.7.2.1. Cough Test....24
3.7.2.2. Wheeze Test....24
3.7.2.3. Forced Expiratory Time....24
3.7.2.4. Maximum Laryngeal Height....24
3.7.2.5. Wheezing on Auscultation....25
3.7.3. Spirometry....25
3.7.3.1. Technique....26
3.7.3.2. Recording of Results....27
3.7.3.3. Type of Spirometer....27
3.7.3.4. Quality Control and Calibration....27
3.7.3.5. Maintenance and Cleaning....28
3.7.3.6. Training of Investigators....28
3.7.4. Operative Variables....28
3.7.4.1. Site of Operation....29
3.7.4.2. Nasogastric Tube Placement Perioperatively....29
3.7.4.3. Length of Operation....29
3.7.4.4. Type of Anesthetic....30
3.8. Outcome Measures....30
3.8.1. Length of Hospital Stay....30
3.8.2. Reference Standard....30
3.9. Ethics....31
3.10. Sample Size....32

3.11. Data Handling and Statistical Analysis..... 32

Chapter 4: Results.....35

4.1. Demographics and Descriptive Statistics..... 35

4.2. Bivariate Analysis..... 39

4.3. Multivariate Analysis..... 44

Chapter 5: Discussion 48

Chapter 6: Conclusions and Recommendations.....52

References.....53

Appendices.....60

Appendix A: Consent Form..... 59

Appendix B: Information Sheet.....61

Appendix C: Participant Data Entry Form.....63

Appendix D: Summary of Acceptability and Reproducibility Criteria for Spirometry (CPSA 1998).....67

Appendix E: Standard Subject Normal Range – Values and Calculations.....68

Appendix F: Equipment Checks Using the Standard Subject..... 69

Appendix G: Examples of Spirometry Calibration.....70

Appendix H: Example of Sketches of Receiver Operator Curves to Determine Cut-points for Dichotomizing Continuous Variables..... 71

Appendix I: Letter of Permission from Excerpta Medica.....72

Appendix J: Letter of Permission from the American Thoracic Society.....73

List of Tables

Table 1.1. Preoperative or operative variables reported to be predictive of postoperative pulmonary complications in studies for which data could not be formatted as 2x2 tables (Fisher *et al.* 2002)..... 8

Table 1.2. Preoperative and operative variables identified as predictors of postoperative pulmonary complications in studies for which data could be formatted as 2x2 tables (Fisher *et al.* 2002)..... 9

Table 1.3. The association between the preoperative history and the occurrence of postoperative pulmonary complications (McAlister *et al.* 2003)..... 11

Table 1.4. The association between the preoperative physical examination and operative factors, and the occurrence of postoperative pulmonary complications (McAlister *et al.* 2003)..... 12

Table 1.5. The association between preoperative laboratory tests and the occurrence of postoperative pulmonary complications (McAlister *et al.* 2003)..... 13

Table 1.6. Variables in final multivariate regression model of McAlister *et al.* (2003) study..... 13

Table 4.1. Participant demographics.....36

Table 4.2. Summary of self-reported smoking history..... 36

Table 4.3. Summary of self-reported health history..... 37

Table 4.4. Summary of physical examination maneuvers..... 37

Table 4.5. Summary of spirometry values..... 38

Table 4.6. Summary of operative variables and outcomes..... 38

Table 4.7. Frequencies of types of operations performed..... 39

Table 4.8. Pulmonary complications breakdown..... 39

Table 4.9. Chi-square and Fisher's exact tests for significance of categorical variables and postoperative pulmonary complications.....40

Table 4.10. Two-independent sample t-tests for significance of continuous variables and postoperative pulmonary complications..... 41

Table 4.11. Chi-square and Fisher's exact tests for significance of newly dichotomized variables and postoperative pulmonary complications..... 41
Table 4.12. Fisher's exact test for significance of alternatively dichotomized Variables and postoperative pulmonary complications..... 42
Table 4.13. Sensitivities, specificities, and odds ratios for all variables and postoperative pulmonary complications after bivariate analysis..... 43
Table 4.14. Final model and parameter estimates after multivariate analysis..... 45

List of Figures

Figure 4.1. Normal Q-Q plot of deviances between observed and expected values..... 46

Figure 4.2. Plot of standardized residuals with case identification..... 47

List of Abbreviations and Nomenclature

Abbreviation	Full Name
BMI	Body Mass Index
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CPSA	College of Physicians and Surgeons of Alberta
DOR	Diagnostic Odds Ratio
FET	Forced Expiratory Time
FEV_1	Forced Expiratory Volume in the First Second
FVC	Forced Vital Capacity
NG	Nasogastric
ROC	Receiver Operator Curve
URTI	Upper Respiratory Tract Infection

List of Definitions (from O'Toole, 1992)

Asthma - A reversible condition marked by recurrent attacks of dyspnea with wheezing due to spasmodic constriction of the bronchi.

Atelectasis - A collapsed or airless state of the lung, which may be acute or chronic, and may involve all or part of the lung.

Chronic bronchitis - The inflammation of one or more bronchi (and possibly trachea), characterized by increased secretion from the bronchial mucosa and obstruction of the respiratory passages.

Chronic emphysema - A pathological accumulation of air in tissues in the lungs developing slowly over a period of years. The terminal bronchioles become plugged with mucous and eventually there is a loss of elasticity in the tissue so that inspired air becomes trapped in the lungs.

Chronic obstructive pulmonary disease (COPD) - A functional category designating a chronic condition of persistent obstruction of bronchial air flow – includes chronic bronchitis and chronic emphysema.

Dyspnea - Laboured or difficult breathing.

Pleural effusion - The accumulation of fluid in the space between the membrane encasing the lung and the membrane lining the thoracic cavity.

Pneumonia - The inflammation of the lungs with consolidation and exudation.

Pneumothorax - The accumulation of air or gas in the pleural cavity, which may result in collapse of the lung on the affected side.

Chapter 1: Introduction

1.1. Background on Postoperative Pulmonary Complications

Pulmonary complications have been reported for many years as frequent complications after surgery and anesthesia. In 1927, perioperative pulmonary morbidity had been sited as affecting approximately 8% of those undergoing surgery (Sise 1927). While the reported incidence of postoperative pulmonary complications since that time has varied between 2% and 46% (Brooks-Brunn 1998, Hall *et al.* 1991, Owings & Kozak 1998, Rao *et al.* 1992, Wightman 1968), it is clear that with an aging population and the increased acuity of patients in tertiary settings, these complications are not on the decline (Graves 1992, King 1991). It has been estimated that nearly 25% of all deaths occurring within the first six days post-surgery are related to pulmonary complications (Brooks-Brunn 1995) and up to two-thirds of all postoperative complications are pulmonary (Ghali 2001). The economic impact of these complications also cannot be ignored. Those people who develop postoperative pulmonary complications have a 96% increase in hospital stay duration and 59% increase in cost of hospitalization (Lawrence *et al.* 1995).

1.2. Lack of Clinical Prediction Rules for Preoperative Evaluation of Pulmonary Risk

Physicians routinely assess patients before surgery to determine their risk for cardiac and pulmonary complications. A clinical prediction rule or predictive index is a "tool that takes the experience of a group of physicians with hundreds or even thousands of patients and distills this experience into a simple rule" (Ebell 2001, p.1). These clinical prediction rules are a convenient and efficient way to apply the best available evidence to patient care and to help physicians make more accurate decisions regarding a patient's diagnosis and/or prognosis (Ebell). F. Macartney (1998) stressed that the usefulness of a method of diagnosis – or in this case, a clinical prediction rule – is measured firstly by

its accuracy and secondly by its brevity. Only once these two attributes are secured can the third important attribute, reliability, be evaluated.

Clinical prediction rules for assessing the risk of cardiac complications after surgery, such as Goldman's Cardiac Risk Index and Detsky's Modified Cardiac Risk Index, have been derived from rigorous and extensive studies and have been tested for their relevance, validity, and usefulness (Ebell 2001). Even though postoperative pulmonary complications are more frequent than cardiac complications, there are far more studies of cardiac risk than pulmonary risk post-surgery (Lawrence *et al.* 1995) Of those studies looking at preoperative risk of pulmonary complications, many have been conducted using inadequate study designs, forcing the reader to question the validity of the results of these studies. Some of these design problems include the inadequate blinding of observers, inadequate sample sizes, retrospective data collection, selection biases, and using clinically unimportant outcomes as the reference standards (Lawrence *et al.* 1989, Williams-Russo *et al.* 1992, Zibrak & O'Donnell 1993). Hence there is a need for high quality prospective studies with independent and blind comparisons of preoperative/operative variables and postoperative outcomes to identify those preoperative variables of greatest utility in predicting postoperative pulmonary complications. Only then can a clinical prediction rule for postoperative pulmonary risk be developed.

1.3. Methodological Features in Diagnostic Studies Which Are Important in Avoiding Bias

Bias in epidemiologic studies can be described as "systematic errors in collecting or interpreting data" (Hennekens & Buring 1987, p. 4). Statistical evaluation can account for chance in studies, but bias is far more difficult to evaluate and therefore must be minimized by using the appropriate study design and conduct (Hennekens & Buring). The ideal design for a diagnostic study is a prospective blind comparison of the test in a consecutive series of participants from a relevant clinical population (Jaeschke *et al.* 1994).

Lijmer *et al.* (1999) empirically assessed diagnostic tests and the impact of faulty design, data collection, and interpretation on the estimates of diagnostic accuracy, mainly diagnostic odds ratios and their antilogarithm transformations. A diagnostic odds ratio (DOR) is the odds for a positive test result in diseased persons relative to the odds of a positive result in non-diseased persons (Kraemer 1992). Appropriate studies on diagnostic tests were identified and observed for associations between study characteristics and estimates of diagnostic accuracy. Statistical comparisons were made using the DORs of studies of a given test that lacked a particular methodologic feature with those without the same shortcomings in design. The examined study characteristics were: case-control vs. cohort studies, different reference tests used for verification of results vs. the same reference tests used on all subjects, partial verification of test results vs. complete verification of all results, non-blinded vs. blinded interpretation of reference test, non-consecutive vs. consecutive inclusion of random participants presenting with the relevant condition, retrospective vs. prospective study designs, and inadequate descriptions of the test under study, study population, and/or reference test vs. detailed descriptions of these characteristics.

Results of the regression analysis from this study indicate that studies of lower methodologic quality generally tend to overestimate the diagnostic performance of a test. The study characteristic that resulted in the highest overestimates of the diagnostic performance of a test (a three-fold overestimate of the DOR) was the use of a case-control study design. When a case-control study design is used, a test is evaluated in a group of participants already known to have the disease and a separate group of participants without the disease, rather than in a relevant clinical population (van der Schouw *et al.* 1995). Mild cases difficult to diagnose are often eliminated resulting in overestimates of sensitivity and specificity (Lijmer *et al.* 1999).

The second-highest overestimates (a two-fold overestimation of the DOR) were found when a different reference test was used for positive and negative test results as opposed to using the same test for both groups. This type of verification bias occurs most often when negative test results are verified using a different and less thorough standard than

the reference test used to verify positive test results (Lijmer *et al.* 1999). This results in an overestimation of sensitivity and specificity of the study test (Lijmer). The term "partial verification bias" is used to describe the situation where more positive test results are verified with the reference test than negative test results (Lijmer *et al.* 1999). This results in either an increase or decrease of the DOR, and an overestimation of sensitivity and underestimation of specificity (Panzer *et al.* 1987).

Two other study characteristics that led to an overestimation of the DORs were inadequate descriptions of definitions of positive and negative test results, and inadequate descriptions of the study population. Detailed descriptions of these characteristics are necessary to allow for generalization, replication, and validation of the study (Jaeschke *et al.* 1994). Likewise, a detailed description of the reference standard and target population is important for diagnostic accuracy. While tests with shortcomings in this area were not shown to distort the DORs higher than the actual number in the Lijmer *et al.* study, this could have been due to difficulties in data abstraction and large interobserver variation in interpreting the reference standard.

Selective inclusion of participants into the study or selecting people for the study in a nonconsecutive manner (selection bias) did not significantly change the estimation of diagnostic accuracy. However, this shortcoming in data collection has the potential to overestimate diagnostic accuracy and should be avoided. An overestimation of a test's accuracy can also occur if there is an interpretation of the reference test with knowledge of the gold standard test (Lijmer *et al.* 1999). The Lijmer *et al.* study did not show there to be a significant change in the DOR of this study characteristic. An explanation for this could be that many of the studies observed had an objective reference standard in which no effect was to be expected. Finally, retrospective data collection as compared to the prospective method of data collection did not result in changed diagnostic accuracy in the Lijmer study.

This study by Lijmer *et al.* emphasizes the importance of using appropriate study design and data collection when conducting a study of diagnosis.

1.4. The Literature on Preoperative Pulmonary Risk Prediction

A systematic review of studies evaluating predictors of postoperative pulmonary complications was conducted by Fisher, Majumdar, and McAlister (2002). Their goal was to evaluate the performance of variables frequently used by clinicians or cited in textbooks/review articles for the prediction of postoperative pulmonary complications in patients undergoing non-thoracic surgery. While they found that over forty variables were used to predict postoperative pulmonary complications, few had ever been evaluated to determine sensitivity, specificity, likelihood ratios and reliability. The systematic review was restricted to high-quality studies based on the criteria found to be important in the Lijmer (1999) study – independent, blind comparisons with a reference standard in an appropriate spectrum of patients. An extensive search of MEDLINE (1966-2001) found only seven high-quality studies with blinded outcome assessments of relevant preoperative/operative variables and outcomes (Ephgrave *et al.* 1993, Fogh *et al.* 1987, Hall *et al.* 1996, Rao *et al.* 1992, Lawrence *et al.* 1996, Mitchell *et al.* 1998, Williams-Russo *et al.* 1992).

Some of the rejected studies, while strong in areas, were lacking in the most crucial factors for determining validity of the study results. Arazolluh *et al.* (2001) conducted a study of large sample size (n = 160,805) and included patients going for various non-cardiac surgical procedures at more than one hundred hospitals involved with the Veterans Affairs National Surgical Quality Improvement Program. In a review of this study, Bradley and McAlister (2002) found that while follow-up was complete for enrolled patients, statistical techniques were justified, and there was adequate validation of their risk model in a separate cohort, some important limitations prevailed. Even though the sample size was large, the sample consisted only of men with high co-morbidity going for "major" surgical procedures, and therefore the generalizability of the results may be limited to a portion of those who go for non-cardiac surgeries. More importantly, the study was not conducted in a blinded fashion: Investigators involved in the outcome follow-up were not blinded to the preoperative status of the individual. This could falsely increase the significance of some individual variables and lead to

larger odds ratios for those variables than is actually the case (Lijmer *et al.* 1999). Another problem with this study is that while many variables of the patient's health history, demographics, and operative factors were tested, virtually all of the data were collected from administrative databases and no data were available on elements of the clinical examination.

Similarly, Brooks-Brunn (1997) conducted a study to determine predictors of postoperative pulmonary complications following abdominal surgery. While this study is an important addition to the rather sparse literature in this area, it cannot be considered a high-quality study of diagnosis. A prospective design was used, and using a split-sample method, the predictive model was validated in another study (Brooks-Brunn 1998). The model building sample appears adequate (n = 400), but was justified based on 16 risk factors while 23 were actually assessed. This sample was described as a "convenience" sample with very little description given as to how this sample was obtained. If this sample was not obtained in a consecutive manner, there is potential for selection bias which, especially in a hospital setting, could incorrectly estimate the true relationship between test variables and outcome (Hennekens 1987). Another area of concern is that details are not given as to which investigators were involved in the collection of preoperative/operative variables, and which investigators were involved in determining the outcome variables; thus it cannot be assumed that this study was conducted in a blinded fashion. Finally, Brooks-Brunn did not include important physical examination maneuvers that are routinely performed.

Sixteen variables were found in the seven high-quality studies to be significantly associated with postoperative pulmonary complications (Fisher *et al.* 2002). These included elements of the patient history (e.g., history of chronic obstructive pulmonary disease, pack-years smoking history), physical examination (e.g., preoperative sputum production), laboratory findings (e.g., abnormal chest x-ray and spirometry), surgical site, duration of anesthesia, and postoperative nasogastric tube placement. Only duration of anesthesia and postoperative nasogastric tube placement were identified in more than one study as being significantly associated with the development of

pulmonary complications after surgery (see Tables 1.1. and 1.2.). There are some concerns regarding the validity and applicability of the variables identified. The sample sizes of these studies were small and the definitions of predictive variables and important pulmonary complications varied (Fisher *et al.* 2002). Also, these studies generally looked at groups of patients going for specific surgeries, mainly abdominal, making these results possibly inappropriate to apply generally to patients undergoing other non-thoracic surgeries (Fisher *et al.* 2002).

There are a few limitations to this systematic review such as the restriction of literature searches to MEDLINE and studies in English. However, this review does reinforce the need for high-quality prospective studies to identify which elements of the patient's history, clinical examination, preoperative laboratory testing, surgery, and anesthesia are independent predictors of postoperative pulmonary complications.

Table 1.1. Preoperative or operative variables reported to be predictive of postoperative pulmonary complications in studies for which data could not be formatted as 2x2 tables.

Variable	Study	*p* Value	Odds Ratio (95% Confidence Interval	Significant in Multivariate Analysis
Smoking history (pack-years)	Rao	<0.01		No
Abnormal results of pulmonary exam*	Lawrence	0.05	5.8 (1.0-32)	Yes
Charlson Comorbidity Score	Lawrence	0.05	1.6 (1.0-2.5)	Yes
Goldman Cardiac Risk Index	Lawrence	0.01	2.0 (1.2-2.6)	Yes
Abnormal Chest Radiograph+	Lawrence	0.04	3.2 (1.1-9.40	Yes
Hypoxia (PaO_2)	Rao	0.01		No
Reduced FEV_1 (% predicted)	Rao	0.009		No
Reduced peak flow (% predicted)	Rao	0.004		No
Type of surgery (abdominal aortic aneurysm repair)	Williams-Russo	<0.001		Yes
Duration of anesthesia	Rao	0.03		No
	Mitchell	<0.001		Yes

*Decreased breathing sounds, prolonged expiration, rales, rhonchi, or wheezes.
+Hyperinflation, pulmonary hypertension, vascular redistribution or edema, atelectasis, effusion, infiltrate, or other parenchymal abnormalities.

NOTE: Table reprinted from the *American Journal of Medicine*, Volume 112, authors Fisher BW, Majumdar SR, and McAlister FA, "Predicting pulmonary complications after non-thoracic surgery: A systematic review of blinded studies", pp. 219-225, 2002, with permission from Excerpta Medica.

Table 1.2. Preoperative and operative variables identified as predictors of postoperative pulmonary complications in studies for which data could be formatted as 2x2 tables.

Variable	Outcome	Studies Identifying Variable	*P* Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Sensitivity	Specificity	Significant in Multivariate Analysis
Preoperative diagnosis of chronic obstructive lung disease	Respiratory insufficiency*	Hall	0.001	4.5	0.75	0.18	0.96	Yes
Preoperative sputum production	Pneumonia, pneumothorax, bronchospasm, respiratory failure, delayed weaning from assisted ventilation, or death	Mitchell	0.005	2.2	0.59	0.56	0.75	Yes
Roizen Dyspnea Score >1	Pneumonia or respiratory failure	Rao	0.01	2.9	0.66	0.44	0.85	Multivariate analysis not done
American Society of Anesthesiologists Score >2	Respiratory insufficiency*	Hall	<0.0001	2.3	0.49	0.65	0.72	Yes
Site of surgical incision (upper abdominal)	Pneumonia, pneumothorax, bronchospasm, respiratory failure, delayed weaning from assisted ventilation, or death	Mitchell	0.0001	4.6	0.37	0.69	0.85	No
Nasogastric tube placement	Pneumonia, pneumothorax, bronchospasm, respiratory failure, delayed weaning from assisted ventilation, respiratory insufficiency or death	Mitchell	<0.0001	5.1	0.23	0.81	0.84	Yes
		Hall	0.001	2.2	0.40	0.73	0.67	Yes

NOTE: Table reprinted from the *American Journal of Medicine*, Volume 112, authors Fisher BW, Majumdar SR, and McAlister FA, "Predicting pulmonary complications after non-thoracic surgery: A systematic review of blinded studies", pp. 219-225, 2002. with permission from Excerpta Medica.

1.5. Summary of Preliminary Study

A study to identify the elements of the preoperative history, physical examination, and operative factors that are of greatest utility in predicting postoperative pulmonary complications after non-thoracic surgeries in patients referred to specialists was recently completed (McAlister *et al.* 2003). In this study, general internists and pulmonologists enrolled consecutive participants with and without pre-existing lung disease and determined the association between pre-operative/operative variables and outcome variables in a blinded fashion. Patients excluded from the study were those less than 18 years of age, those with a history of sleep apnea or need for mechanical ventilation, those with neuromuscular diseases such as Muscular Dystrophy and Parkinson's Disease, those undergoing cardio thoracic surgeries, and those who were cognitively impaired.

Data on participants' demographics and medical history were collected and included age, gender, height, weight, smoking status (including total number of pack-years smoked), upper respiratory tract infection within four weeks of planned surgery, history of bronchospastic airway disease, presence/absence of daily cough (dry vs. productive), and exercise capacity. Data from a standardized physical examination were also collected and included a cough test, wheeze test, forced expiratory time, maximum laryngeal height, and the presence/absence of wheezing in the lungs on auscultation. Spirometry tests, chest x-rays, and arterial blood gases were performed on participants only when it was part of their regular preoperative work-up. Operative variables including duration of surgery, site of operation, elective vs. urgent surgery, and type of anesthesia, were obtained from the patients' charts after discharge.

The outcome measures - a symptomatic and clinically significant postoperative pulmonary complication prior to hospital discharge or postoperative day seven (whichever came first) - were obtained from the patients' charts by another researcher blinded to their preoperative and operative status using standardized definitions. These pulmonary complications were defined using a hierarchy of severity. They were, in

decreasing order of severity: death from respiratory causes, respiratory failure requiring mechanical ventilation, pneumonia, atelectasis of lung or lobe requiring intervention, pneumothorax or pleural effusion requiring intervention, and delayed weaning from assisted ventilation. Only the most serious occurrence for each patient was recorded.

Out of the 272 participants enrolled, 22 suffered a postoperative pulmonary complication – six respiratory failures requiring assisted ventilation, nine pneumonias, and seven atelectases requiring intervention. Many variables were found to be statistically significant after bivariate analysis (see Tables 1.3. -1.5.). However, only three remained significant after multivariate analysis. These variables were: age greater than or equal to 65 years, smoking history of greater than or equal to 40 pack-years, and a maximum laryngeal height of less than four centimetres (see Table 1.6.).

Table 1.3. The association between the preoperative history and the occurrence of postoperative pulmonary complications.

Variable	Number of Patients with a Particular Finding (n = 272)	Odds Ratio (95% Confidence Interval)	*p* Value
Age of ≥ 65 years	140	4.7 (1.6-14.4)	0.006
Male	108	1.03 (0.6-1.8)	0.91
Ever smoked (versus never smoked)	153	2.2 (0.8-5.8)	0.16
Current smoker (within 2 weeks of operation)	52	0.7 (0.2-2.3)	0.69
Smoked ≥ 40 pack-years	42	5.7 (2.3-14.2)	0.0002
Recent (within 4 weeks) upper respiratory tract infection	32	0.7 (0.2-3.3)	0.95
History of COPD	32	4.2 (1.6-11.3)	0.007
History of asthma	29	2.0 (0.6-6.4)	0.41
Daily productive cough	30	1.9 (0.6-6.1)	0.45
Exercise capacity of ≤ two blocks or one flight of stairs	41	3.0 (1.1-7.8)	0.05

NOTE: Table reprinted from the *American Journal of Respirratory and Critical Care Medicine*, Volume 167, authors McAlister FA, Khan NA, Straus SE, Papaioakim M, Fisher BW, Majumdar SR, Gajic O, Daniel M, and Tomlinson G, "Accuracy of the preoperative assessment in predicting pulmonary risk after nonthoracic surgery", pp. 741-744, 2003, with permission from the American Thoracic Society.

Table 1.4. The association between the preoperative physical examination and operative factors, and the occurrence of postoperative pulmonary complications.

Variables	Number of patients with a Particular Finding (n = 272)	Odds Ratio (95% Confidence Interval)	*p* Value
Preoperative physical examination:			
Body mass index of ≥ 30	101	4.1 (1.6-10.4)	0.004
Positive cough test	26	4.3 (1.5-12.3)	0.01
Positive wheeze test	31	3.4 (1.2-9.4)	0.04
Forced expiratory time of ≥ 9 seconds	42	5.7 (2.3-14.2)	0.0002
Maximum laryngeal height of ≤ 4 cm	37	6.9 (2.7-17.4)	< 0.0001
Wheezing on standard auscultation	21	3.1 (0.9-10.0)	0.13
Operative factors:			
Upper abdominal incision	24	1.0 (0.2-4.7)	0.73
General anesthesia	222	2.4 (0.5-10.5)	0.38
Duration of operation ≥ 2.5 hours	75	2.9 (1.2-7.0)	0.03

NOTE: Table reprinted from the *American Journal of Respirratory and Critical Care Medicine*, Volume 167, authors McAlister FA, Khan NA, Straus SE, Papaioakim M, Fisher BW, Majumdar SR, Gajic O, Daniel M, and Tomlinson G, "Accuracy of the preoperative assessment in predicting pulmonary risk after nonthoracic surgery", pp. 741-744, 2003, with permission from the American Thoracic Society.

Table 1.5. The association between preoperative laboratory tests and the occurrence of postoperative pulmonary complications (McAlister *et al.* 2003).

Variable	Number of Patients with a Particular Finding	Odds Ratio (95% Confidence Interval)	*p* Value
Had spirometry performed	145	0.84 (0.53-1.35)	0.78
FEV_1 < 1 L/min*	10	7.90 (1.7-37.0)	0.02
FVC < 1.5 L/min*	8	11.1 (2.2-56.4)	0.005
Had arterial blood gases performed	66	0.7 (0.3-1.8)	0.61
$Pco_2 \geq 45$ mm Hg†	3	61.0 (3.8-986.4)	0.001
$Po_2 < 75$ mm Hg†	14	13.4 (1.3-14.1)	0.008
Had chest radiography performed	124	1.1 (0.7-1.7)	0.83
Chest radiography abnormal‡	21	1.7 (0.6-4.9)	0.40

*Among the 145 participants who had spirometry performed.
†Among the 66 participants who had arterial blood gases performed.
‡ Among the 124 participants who had chest radiography performed.

NOTE: Table reprinted from the *American Journal of Respirratory and Critical Care Medicine*, Volume 167, authors McAlister FA, Khan NA, Straus SE, Papaioakim M, Fisher BW, Majumdar SR, Gajic O, Daniel M, and Tomlinson G, "Accuracy of the preoperative assessment in predicting pulmonary risk after nonthoracic surgery", pp. 741-744, 2003, with permission from the American Thoracic Society.

Table 1.6. Variables in final multivariate regression model of McAlister *et al.* study.

Variable	Odds Ratio	*p* Value
Age ≥ 65 years	1.8	.02
Smoked ≥ 40 pack- years	1.9	.02
Maximum laryngeal height < 4 centimetres	2.0	.007

Laboratory testing variables were not included in the multivariate analysis.

NOTE: Table reprinted from the *American Journal of Respirratory and Critical Care Medicine*, Volume 167, authors McAlister FA, Khan NA, Straus SE, Papaioakim M, Fisher BW, Majumdar SR, Gajic O, Daniel M, and Tomlinson G, "Accuracy of the preoperative assessment in predicting pulmonary risk after nonthoracic surgery", pp. 741-744, 2003, with permission from the American Thoracic Society.

Thus, people at increased risk for postoperative pulmonary complications following non-thoracic surgeries can be identified using preoperative variables. However, this prediction model needs to be validated in an independent data set (Ebell 2001). Another limitation of this study is the inherent selection bias. The sample patients were all

referred to general internists and were likely a "sicker" population than the "average" population that undergoes elective non-thoracic surgeries. Spirometry and arterial blood gas determination was also not performed on all subjects due to cost constraints and therefore the analysis of these variables was based on small numbers and may not be accurate. To develop and validate a multivariable risk index for predicting postoperative pulmonary complications following non-thoracic surgeries, a large prospective cohort study in a general preoperative population of consecutive subjects that all undergo spirometric testing needs to be performed.

Chapter 2: Study Objectives and Hypothesis

2.1. Study Objectives

The first objective of this study was to determine the accuracy of selected elements of the history, physical examination, routine preoperative tests, and operative factors for predicting postoperative pulmonary complications in participants undergoing non-thoracic surgical procedures.

The second objective was to derive a multivariate index for predicting postoperative pulmonary complications in participants undergoing non-thoracic surgical procedures.

2.2. Hypothesis

This study evaluates the proposition that people at risk for developing postoperative pulmonary complications can be identified using a multivariate risk index of selected preoperative and operative variables. Therefore, the *null hypothesis* for this study is as follows:

Preoperative and operative assessment variables cannot be used to identify people who are greater than average at risk of developing pulmonary complications after non-thoracic surgery.

Chapter 3: Methods

3.1. Study Design

This is a prospective cohort study. Preoperative and operative data were collected on participants before their planned surgeries and data on the presence or absence of post-surgical pulmonary complications were collected on these participants after their hospital stay. The investigators observed the natural course of events that each participant experienced with no involvement in their diagnosis, care, or recovery.

3.2. Setting

This study was conducted at the University of Alberta Hospital. Preoperative data were collected in the Pre-Admission Clinic, and operative factors and outcome data were collected by reviewing the participants' charts in Medical Records after their discharge from the hospital.

3.3. Timeline

Data collection in the Pre-Admission Clinic began in May, 2001 and concluded in August, 2002. Data collection in Medical Records extended through January, 2003.

3.4. Data Collectors

The collection of data in the Pre-Admission Clinic was performed by three individuals (two medical students and one registered nurse) who were trained in proper data collection techniques. These individuals met to discuss techniques and physical examination maneuvers to ensure consistent and accurate reporting. Data collection in Medical Records was performed by three trained individuals familiar with the hospital chart lay-out (medical student, resident, and registered nurse). These assessors were unaware of the preoperative assessments and were not involved with the care of the

patient. The preoperative, operative, and postoperative variables were all rigorously defined and standard definitions were used by all.

3.5. Study Participants

3.5.1. Inclusion Criteria

Adults aged 17 years and older were approached to participate in the study while attending the Pre-Admission Clinic in preparation for elective surgery. At this location, 17 year olds are considered as adult patients and spend their duration of post-operative hospital stay on the various adult surgical wards. For these two participants, parental consent was also obtained.

Potential participants were approached by the researcher in consecutive order of their appointment times at the clinic. However, this order was subject to change due to the availability of the patients during this time. The preoperative data collection occurred Monday through Friday to obtain a broad spectrum of participants booked for various surgical procedures.

The participants included patients with or without pre-existing lung disease at the time of initial assessment. This information was obtained during the interview when the participant was asked questions regarding health history, which may include chronic obstructive lung disease and/or asthma.

3.5.2. Exclusion Criteria

Specific exclusion criteria of participants were defined at study initiation and included:

1. Patients scheduled for intra-thoracic surgeries. These surgeries included heart or lung surgeries such as coronary artery bypass surgeries, lung biopsies, lung resections, thoracotomies, and esophageal surgeries. Because these surgeries

involve trauma to the thoracic area, pulmonary complications are more common than with non-thoracic surgeries and are often due to the surgery itself and not necessarily to the preoperative risk factors (Thelan *et al.* 1994).

2. Patients on any kind of mechanical ventilation at the time of pre-operative assessment. These patients would require mechanical ventilation postoperatively and could not be subject to the same outcome measures criteria as non-ventilated participants. Patients with a documented history of sleep apnea were also not approached to participate in the study for the same reason. Many people with sleep apnea use a device while sleeping at night called a nasal continuous positive airway pressure (CPAP) device, or one similar to it, to prevent the occlusion of the airway (Lewis & Collier 1992).

3. Patients with a neuromuscular disease. These diseases included Parkinson's Disease, Amyotrophic Lateral Sclerosis, Multiple Sclerosis, Huntington's Disease, and others. Complications from these diseases often include respiratory infection secondary to compromised lung function or dysphagia leading to aspiration (Lewis & Collier 1992). It would have been inappropriate to have these patients as participants in the study as it would be difficult to ascribe a postoperative pulmonary complication to preoperative or operative variables rather than to the disease process itself.

4. Patients with any medical problem or cognitive impairment that would inhibit their participation in any portion of the preoperative history, physical examination, and/or spirometry. For example, a preoperative patient using a tracheostomy stoma to breath would not be able to perform the spirometry tests adequately (using our equipment), or a patient with severe cognitive impairment would have difficulty understanding the questionnaire on health history and would have difficulty comprehending the method of performing the spirometry maneuvers.

5. Finally, participants were excluded from the study if they did not subsequently undergo the planned surgery.

3.5.3. Refusals

Fourteen of the 758 people who were approached to participate in the study refused (1.8%). Ten of those were female and four were male. One male participant requested to be taken out of the study after the surgery was performed. No reason was given for his decision to drop out. All others refused initially when approached in the Pre-Admission Clinic.

3.6. Consent and Data Collection Forms

3.6.1. Consent Form and Information Sheet

After being given a detailed explanation of the study by the investigator, a consent form was presented to the participant to sign (Appendix A). Only if all questions in part two of the form were answered "yes" did the interview continue. All participants were given an information sheet summarizing the study to take home (Appendix B). These forms were developed for the preliminary study and were modified for the current study.

3.6.2. Data Collection Form

All data collected on the participants were recorded on the participant data entry form (Appendix C). Data on oxygen saturation on room air, arterial blood gases on room air, and chest X-ray were not collected, while data on nasogastric tube placement perioperatively and internal medicine consultation pre-operatively were added.

3.7. Procedures

The variables collected in this study were chosen because they have been shown to be associated with postoperative pulmonary complications in at least one study in the systematic review of the literature or the pilot study. In addition to being associated with postoperative pulmonary complications, these variables are relatively simple to obtain during the preoperative visit and do not require invasive procedures.

3.7.1. History

This information was obtained by interview with the participant. These variables include age, gender, body mass index, smoking status and number of pack-years smoked, recent upper respiratory tract infection, history of bronchospastic airway disease, daily cough, and exercise capacity.

3.7.1.1. *Age*

Each participant's age was recorded in years. This variable is of interest because changes to the structure of the respiratory system occurs during the natural aging process, decreasing, for instance, a person's ability to cough effectively (Lewis & Collier 1992). This may put the elderly patient at greater risk for developing pulmonary complications after surgery.

3.7.1.2. *Gender*

Gender is a biologically important variable that should always be included in a cohort study.

3.7.1.3. *Height and Weight*

The participant's height and weight were recorded in centimetres and kilograms, respectively. These values were used to calculate body mass index (BMI) which is a frequently used measurement for determining ideal weight range and obesity. The calculation for BMI is as follows:

$$BMI = \text{weight (kg)} \div \text{height}^2(\text{m}^2)$$

According to Health Canada guidelines, a BMI of less than 18.5 is considered underweight, 18.5 to 24.9 is considered normal, 25 to 29.9 is considered overweight, and 30 or greater indicates obesity (Health Canada website). Respiratory problems can be a complication of obesity as large deposits on the abdomen and chest impede the movement of the muscles of the chest wall (Lewis & Collier 1992). Ambulating after surgery may also be more difficult, increasing the chances of atelectasis.

3.7.1.4. *Smoking Status*

Each participant was asked if he or she has ever smoked. If the answer was "yes", then he or she was asked on average how many packs of cigarettes were smoked in a day and for how many years. The investigator was able to calculate pack-years smoked by multiplying these two numbers. If the participant had quit smoking, the number of months ago he or she had quit was recorded. If the participant had quit smoking less than two months ago, then the number of weeks ago was recorded. Pipe and cigar smokers were not included as smokers for this study.

Cigarette smoking is the most important cause of chronic bronchitis (Crompton 1995). Reduced ciliary activity of cells in the respiratory tract, increased production of mucous secretions, and reduced airway diameter are significant results of cigarette smoking leading to chronic bronchitis (Lewis & Collier 1992). After discontinuation of smoking, the decline in pulmonary function slows, and the "cessation of smoking, even 24 hours

before surgery, improves mucociliary function, mucous clearance, and oxygenation as a result of decreased carbon monoxide levels" (Lewis & Collier 1992, p 603).

3.7.1.5. *Recent Upper Respiratory Tract Infection*

Each participant was asked if he or she had an upper respiratory tract infection (URTI) within the last four weeks. This was explained as a "cold" or a "flu with cough, sore throat, and/or nasal discharge". If the participant replied "yes" to this question, he or she was then asked if the infection was less than two weeks ago or two to four weeks ago. Chest infections are a possible complication of an URTI and recovery time can take up to two to three weeks (Lewis & Collier 1992).

3.7.1.6. *Self-Reported History of Chronic Obstructive Pulmonary Disease*

Each participant was asked if he or she had chronic obstructive pulmonary disease (COPD) or if he or she had been told previously by a physician that he or she had emphysema, chronic bronchitis, or obstructive airway disease. They were also asked if they had been using bronchodilators or "inhalers" chronically for any of these diseases. If the response was "yes" to either question, then they were asked if the COPD was inactive or active at the time of the interview. Pneumonia is one of the most frequent complications of COPD and this risk is increased after surgery (Lewis & Collier 1992).

3.7.1.7. *Self-Reported History of Asthma*

Each participant was asked if he or she had asthma or if he or she had been told previously by a physician that he or she had asthma or reversible obstructive airway disease. They were also asked if they were using bronchodilators or inhaled steroids for asthma. If the response was "yes" to either question, then they were asked if the asthma was inactive or active at the time of the interview. Pneumonia has also been cited as a complication of chronic asthma, as well as pneumothorax and atelectasis (Lewis &

Collier 1992). The patient with chronic asthma may be more at risk of developing these complications after undergoing a surgical procedure.

3.7.1.8. *History of a Daily Cough*

The participant was asked if he or she regularly coughed throughout or during any point in the day. If they replied "yes", they were then asked if the cough was usually dry or productive. The presence of a cough may be a principal symptom of respiratory disease.

3.7.1.9. *Exercise Capacity*

The participant was asked if he or she could walk two blocks or take one flight of stairs without growing short of breath and having to stop. If participants replied that they could walk two blocks, but could not take the flight of stairs without growing short of breath (or vice versa), this was still recorded as a "yes", namely that the participant was able to do so. This dyspnea-limited exercise tolerance of less than two blocks or a flight of stairs corresponds to the levels of two and higher on the frequently used Roizen Dyspnea Score (Fan *et al.* 1987). Dyspnea on exertion is non-specific, but can be indicative of respiratory disease (Ford & Nixon 1995), cardiovascular disease or deconditioning.

3.7.2. Physical Examination

The investigator observed five physical examination maneuvers during the preoperative visit in the Pre-Admission Clinic. These maneuvers were the cough test, wheeze test, forced expiratory time, maximum laryngeal height, and wheeze on auscultation.

3.7.2.1. *Cough Test*

The participant was asked to take a deep inspiration and cough once. The test was defined as positive if the cough was followed by further coughing, or resulted in crackles or wheezes heard by the unassisted ear.

3.7.2.2. *Wheeze Test*

This test was performed by having the participant take five deep inspirations and expirations and then auscultating (listening with a stethoscope) for wheezes between the shoulder blades posteriorly. The test was positive if wheezing was present. Wheezing is a sound produced by the passage of air through narrowed bronchi (Crompton 1995).

3.7.2.3. *Forced Expiratory Time*

With the participant sitting upright, he or she was asked to take in as deep a breath as possible and blow it out through an open mouth as hard and as fast as possible, breathing out until the lungs felt completely empty. Before the participant began to exhale, the investigator placed the bell of the stethoscope over the trachea in the suprasternal notch. As soon as the participant began to exhale, the investigator timed to the nearest second the duration of audible exhalation. Two runs of the forced expiratory time (FET) were made for each participant and the fastest result was recorded. A value of greater than or equal to nine seconds is considered abnormal and has been shown to be an indicator of obstructive airway disease (Straus *et al.* 2002).

3.7.2.4. *Maximum Laryngeal Height*

Maximum laryngeal height is the distance between the top of the thyroid cartilage and the suprasternal notch at the end of expiration. The participant was asked to sit upright and look straight ahead with hands relaxed on his or her lap. When the participant reached the end of expiration, the space between the top of the thyroid cartilage and

suprasternal notch was measured. A video clip demonstrating the proper method for this maneuver was available on the pilot study website and was viewed by each investigator before initiating the data collection. An abnormal value is defined as four centimetres or less and has been shown to be indicative of obstructive airway disease (Straus *et al.* 2000).

3.7.2.5. *Wheezing on Auscultation*

On deep respiration, the participant's lungs were auscultated on the bilateral upper and lower back while the chest was exposed. Any expiratory wheezes heard in any of the four areas was considered a positive test.

3.7.3. Spirometry

Spirometry is the "measurement of volume change during various clearly defined breathing maneuvers" (Miller 1987). It is a useful screening test of general lung function and can be used to assist in the assessment of respiratory diseases such as COPD, asthma, and chronic bronchitis (College of Physicians and Surgeons of Alberta [CPSA] 1998).

The spirometric parameters of interest for this study were forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and the ratio between the two as a percentage (FEV_1/FVC x 100%). FVC is the "maximum expiration made as rapidly as possible after a maximum inspiration" (Miller 1987), and FEV_1 is the "maximum volume that can be expired from a full inspiration in one second" (CPSA 1998).

The spirometry tests were performed after the history and physical examination were recorded. The participant did not use any bronchodilators during this time.

3.7.3.1. *Technique*

Obtaining accurate spirometric values is dependent on the effort, understanding, and coordination of the participant. This requires active coaching before and during the test. The following is an example of instructions the investigator gave to the participant (adapted from CPSA 1998 guidelines):

Pre-test Instructions

"This is a test that will require your maximal effort."

"After placing the nose clamps over your nose, I am going to ask you to fill your lungs as much as possible."

"Then, after placing the mouthpiece in your mouth and creating a tight seal, I will tell you to completely empty your lungs as fast as you can. This will require you to use the muscles in your chest and stomach."

"I will then repeat the instructions as you go through the test."

Instructions During the Participant's Performance of the Test

With the participant breathing normally;

"After the next breath I want you to fill your lungs as much as possible. Take a big breath in-in-in, keep inhaling."

At total lung capacity and after mouthpiece is in place;

"Blow-blow-blow, keep blowing, keep blowing until you can't blow out any more air."

"Come off the mouthpiece and rest."

"We will be doing this a few more times."

The investigator observed for any discomfort during the procedure. The participant was also requested to tell the investigator if, at any stage during the procedure, they were experiencing pain, dizziness, or discomfort. The test was then terminated. All participants performed the spirometry procedures while sitting as erect as possible.

3.7.3.2. *Recording of Results*

The spirometry testing for each individual continued until the two highest values for FEV_1 and FVC were in agreement within two hundred millilitres. A minimum of three tests were performed. The highest values for FEV_1 and FVC were recorded if all criteria were met and regardless if they were from the same test. A summary of the acceptability and reproducibility criteria used by the College of Physicians and Surgeons of Alberta and followed during this study is shown in Appendix D. Printouts of the best two tests, including values and flow-volume displays, were attached to the participant entry forms.

3.7.3.3. *Type of Spirometer*

The spirometer used in this study was a "Pony" hand-held, portable, pneumotach spirometer which used an open circuit system to make measurements. This "pneumotach" system uses a sensitive manometre to measure instantaneous air flow by detecting the air pressure drop across a slight resistance (Dawson 1984). Disposable tubular mouthpieces were used with this machine.

3.7.3.4. *Quality Control and Calibration*

Checks were done routinely to test the investigator's technique and equipment. The normal range for a "standard subject" was determined following the guidelines outlined by the CPSA (Appendix E). This standard subject performed spirometry on a weekly basis and the values were recorded (Appendix F).

Calibration of the instrument occurred only when necessary. However, the instrument was checked daily for the possible need for calibration (CPSA 1998). With the assistance of technicians in the Pulmonary Function Laboratory at the University of Alberta Hospital, a three litre, syringe-like device that produced digital results was used to measure the accuracy of the measurement of FVC by the spirometry machine. The

universal guidelines accepted by the CPSA recommend that the output should read three litres plus or minus three percent or ninety millilitres. Appendix G presents some of these values obtained throughout the duration of the study. According to the CPSA guidelines, calibration of the instrument was not necessary during the duration of the study. However, the instrument was calibrated on December 13, 2001 and February 28, 2002 as the error was nearing three percent.

3.7.3.5. *Maintenance and Cleaning*

Maintenance and cleaning of the spirometer was done routinely and according to the manufacturer's and universal guidelines (CPSA 1998). Mouthpieces were disposable, and all other equipment was swabbed with alcohol after each participant use.

3.7.3.6. *Training of Investigators*

Spirometry tests may be conducted by those who meet the criteria for Level I testing (CPSA 1998). Level I technicians are "persons trained in, and with demonstrated ability to perform spirometry" (CPSA). The tests were reviewed by a qualified physician for quality, and feedback was given to the investigator on an ongoing basis.

3.7.4. Operative Variables

Data on operative variables were collected by the investigators JB and KB from the patients' charts after their discharge from the hospital. These variables were: site of operation, nasogastric tube placement perioperatively, length of operation, and type of anesthetic. The charts were also reviewed for internal medicine consultations preoperatively and the duration of hospital stay. Because the preliminary study involved only patients who visited an internal medicine physician preoperatively, this variable was of interest for this study.

3.7.4.1. *Site of Operation*

The site of operation was obtained from the discharge summary and operating room records. The operative sites were categorized *a priori* as upper abdominal (above umbilicus), lower abdominal (umbilicus and below, including inguinal), laparoscopic intra-abdominal, orthopedic (lower limbs, upper limbs, and back), arthroscopic orthopedic, urologic, neurosurgical (cerebral and spinal), and other (ears-nose-throat surgeries, plastic surgeries, opthalmological surgeries, and any other surgery not falling under the mentioned categories). Operations including the kidney were considered as upper abdominal surgeries and open resections of the bladder or prostate were considered as lower abdominal surgeries. Upper abdominal surgery has been noted in the literature to increase the risk of pulmonary complications after surgery on bivariate analysis (Mitchell *et al.* 1982). Alterations to the gastrointestinal tract after surgery that can lead to pain and discomfort are more pronounced after abdominal surgery, and this pain and discomfort can impede deep breathing which helps to prevent alveolar collapse and the stasis of secretions in the narrower airway passages (Lewis & Collier 1992).

3.7.4.2. *Nasogastric Tube Placement Perioperatively*

Nasogastric (NG) tube placement perioperatively has been indicated as a potentially important variable associated with the development of postoperative pulmonary complications (Mitchell *et al.* 1998). Mitchell et al. suggest that the tube placement may "interfere with effective coughing postoperatively because of incomplete closure of the glottis, or that bacteria "may be more easily transferred from the oral pharynx to the lung", increasing the risk for pneumonia (p.197).

3.7.4.3. *Length of Operation*

The length of operation, recorded in hours and obtained from the operating room logs, is of interest because duration of anesthesia has been cited as a potentially important risk factor for lung complications after surgery (Rao 1992). The failure of maximal

ventilation while under the effects of anesthesia may contribute to lung atelectasis and infection, with this risk increasing with prolonged duration under anesthesia (Rao, Lewis & Collier 1992).

3.7.4.4. *Type of Anesthetic*

General anesthetic, compared to spinal and local anesthetics, has been cited as a potential predictor of postoperative pulmonary complications (Arozullah 2001). General anesthesia is usually the choice of anesthesia for more lengthy surgical procedures and, because adjuncts such as muscle relaxants or hypnotics are usually administered at the same time, there is a risk of respiratory depression and airway obstruction (Lewis & Collier 1992).

3.8. Outcome Measures

3.8.1. Length of Hospital Stay

Participants' length of stay in the hospital was recorded in days. This variable was of interest because determining the significance (or insignificance) between postoperative pulmonary complications and length of stay in hospital would either strengthen or weaken the argument that pulmonary complications after surgery result in an increase in hospital stay.

3.8.2. Reference Standard

The reference standard for this study was the development of pulmonary complications after surgery. Studies have used various definitions of postoperative pulmonary complications with varying degrees of clinical significance (Fisher *et al.* 2002). For this study, a positive outcome measure was the experience of a symptomatic and clinically significant postoperative pulmonary complication prior to hospital discharge or postoperative day seven (whichever came first). There was the assumption that any

clinically significant abnormalities would be noted by the participants' attending physicians in the appropriate manner. The physicians diagnosing these outcomes were unaware of the participant's involvement in this study or the results of our preoperative assessment.

Postoperative pulmonary complications were defined as follows, with only the most serious occurrence in the hierarchy noted for each participant with the outcome:

1. Death (cause of death recorded)
2. Respiratory failure requiring mechanical ventilation
3. Pneumonia, defined using the Centers for Diseases Control and Prevention definition; "crackles and dullness to percussion on physical examination of the chest or chest x-ray showing new or progressive infiltrative consolidation or cavitation, AND any of the following: new onset purulent sputum or change in character of sputum, organism isolated from blood culture, or isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy" (Garner *et al.* 1988)
4. Atelectasis of lung or lobe requiring bronchoscopic intervention
5. Pneumothorax or pleural effusion requiring intervention (drainage)
6. Delayed weaning from assisted ventilation of $\geq$ 48 hours after surgery

3.9. Ethics

The study protocol was approved by the Health Research Ethics Board of the University of Alberta Hospital, Edmonton. Copies of the consent form, information sheet, and participant entry form are included as Appendices A, B, and C.

3.10. Sample Size

Sample size for this study was determined using the formula (Daniel 1999):

$$n = \frac{Z^2\alpha_{(2)}pq}{\delta^2}$$

where Z is the 2-tailed normal deviate (in this case 1.96)
p and q are the expected sampling proportions
and δ is the desired sampling error (for this study, 0.01)

An estimate of a 3% (p = .03, q = .97) postoperative pulmonary rate after non-thoracic surgeries was made after examining administrative data over a two year period of time (Ghali 2001). A sample size of 1,118 was adequate to estimate an incidence of postoperative pulmonary complications of 3% with ±1% error. However, owing to limited time in obtaining the desired sample size, this analysis is limited to 745 persons in this thesis. Data collection continues and the full sample is expected to be obtained later in 2003.

3.11. Data Handling and Statistical Analysis

Participant data were entered into an SPSS database and an Excel (for verification and dialogue entry) database. The data set was analyzed using SPSS for Windows version 10.0. There were 55 participants who had missing data on nasogastric tube placement.

The study population demographics were examined by determining frequencies of occurrence for categorical variables and means, ranges, and standard deviations for continuous variables. FEV_1 - % predicted was calculated using the Crapo *et al.* (1981) predictive equations because it has been considered a useful value in evaluating lung function. These equations are as follows:

FEV_1 - % Predicted for Males = 0.0414(Height) – 0.0244(Age) – 2.190
FEV_1 - % Predicted for Females = 0.0342(Height) – 0.0255(Age) – 1.578

The proportion of pulmonary complications was determined and then further broken down into the frequency of occurrence of each complication.

The Chi-square test or Fisher's exact test was used to evaluate the relationships between dichotomous variables and postoperative pulmonary complications. These same two tests were also used to test for trend for categorical variables. Fisher's exact tests were used when 80% of the expected cell frequencies in the 2x2 or 2xn tables were not > 5. The relationships between continuous variables and pulmonary complications were tested using the two-independent sample *t*-test (or the Mann-Whitney *U*-test if the Levene's test for equality of variances was not satisfied). Histograms of continuous variables (displayed as those without and with pulmonary complications) were created to observe for normality. These continuous variables were then dichotomized using cut-points (delineating "normal" and "at risk") which are commonly used in the literature, for clearer and more useful interpretation. Further, receiver-operator curves (ROCs) were used to determine whether new cut-points for these variables would be more appropriate. These newly dichotomized variables were then evaluated for significance and, if close to the later cut-points, the universally accepted cut-points were used in the multivariate analysis.

Based on the results of these bivariate tests for significance, a multivariate logistic regression was fit using the "purposeful selection" method described by Hosmer and Lemeshow (2000). All variables with a $p < 0.20$, as well as those believed to be clinically important, were entered into the model. Using Wald statistics, variables not statistically significant at this point (i.e. $p > 0.05$) were removed from the model. The likelihood ratio test was then used to verify that the removed variables were not significant. At this point, continuous variables in the model were tested for linearity and replaced with a categorical variable if not linear. This was done by creating new categorical variables by determining quartiles for the continuous variables and fitting a logistic model with the categorical variable as an independent variable. The estimated Beta coefficients for the categorical variables were then plotted against the quartile midpoints and, if the plots appeared to be linear, then the variable could be

kept as a continuous variable. All clinically plausible first order interactions were then entered into the model, one at a time, to determine significance (identified using Wald statistics). A final model was achieved after performing the likelihood ratio test to assess the significance of variables removed in the interactions. Finally, the Hosmer-Lemshow test was applied to assess the fit of the new model.

Chapter 4: Results

4.1. Demographics and Descriptive Statistics

Thirty-two out of 777 participants did not have their charts available for operative factors and outcome determination and could not be used in this study. Out of the remaining 745 participants, 55 had information on nasogastric tube placement that was not recorded.

There were almost equal numbers of males and females in the study with 359 (48.2%) males and 386 (51.8%) females. The mean age for males was 55.5 years, and 53.1 for females. Frequencies of the categorical variables and means, ranges, and standard deviations of the continuous variables are summarized in Tables 4.1. - 4.7.

There was a total of 20 postoperative pulmonary complications. Since there were 745 participants in the study, the incidence of pulmonary complications was 2.68%. A breakdown of the frequencies of the hierarchical categories of pulmonary complications is shown in Table 4.8. with there being one death, two respiratory failures, five pneumonias, four atelectases, one pneumothorax or pleural effusion, and seven delayed weanings from assisted ventilation.

Table 4.1. Participant demographics n = 745 [Males = 359 (48.2%), Females = 386 (51.8%)]

Variable	Gender	Mean	SD	Min	Max	Quartiles 25th	50th(Median)	75th
Age		54.2	16.6	17	91	41	55	67
(yrs)	M	55.5		17	88			
	F	53.1		17	91			
Height		170.5	9.7	148	201	163	171	178
(cm)	M	177.3		153	201			
	F	164.1		148	185			
Weight		79.9	18.9	41	160	67	78	91
(kg)	M	86.5		50	160			
	F	73.8		41	150			
BMI		27.4	5.9	15	52	23	27	30
	M	27.5		16	46			
	F	27.4		15	52			

BMI=body mass index, SD=standard deviation

Table 4.2. Summary of self-reported smoking history (n = 745)

Variable	Total (%)	Mean	Min	Max	Quartiles 25th	50th(Median)	75th
Ever smoked	442 (59)						
Number of pack-years smoked (n=442)		19.5	.5	100	0	3.5	19.0
Still smoking	172 (23)						
Quit smoking:	270 (36)						
>12 months ago	228						
6-12 months ago	11						
2-6 months ago	17						
<2 months ago	14						
*If quit smoking <2 months ago, # of weeks quit:							
1 week	4						
1.5 weeks	1						
2 weeks	2						
3 weeks	1						
4 weeks	2						
5 weeks	2						

*Data missing for 2 participants; therefore total does not equal 14

Table 4.3. Summary of self-reported health history (n = 745)

Variable	Total (%)
Recent URTI	115 (15.4)
If "yes" to recent URTI:	
2-4 weeks ago	45
<2 weeks ago	70
History of COPD	34 (4.6)
If "yes" to history of COPD:	
Currently active	14
Currently inactive	20
History of asthma	68 (9.1)
If "yes" to history of asthma:	
Currently active	29
Currently inactive	39
History of a daily cough	133 (17.9)
If "yes" to history of a daily cough:	
Cough dry	72
Cough productive	61
Exercise capacity:	
≥1 flight of stairs or 2 blocks	670 (89.9)
<1 flight of stairs or 2 blocks	75 (10.1)

Table 4.4. Summary of physical examination maneuvers (n = 745)

Variable	Total (%)	Positive (%)
Cough test		57 (7.7)
Wheeze test		26 (3.5)
Forced expiratory time:		
<9 seconds	724 (97.2)	
≥9 seconds	21 (2.8)	
Maximum laryngeal height:		
>4 centimetres	639 (85.8)	
≤4 centimetres	106 (14.2)	
Wheeze on auscultation		23 (3.1)

Table 4.5. Summary of spirometry values (n = 745)

Variable	Mean	Minimum	Maximum	Quartiles		
				25th	50th(Median)	75th
FEV_1 (litres)	2.6	0.7	5.1	2.01	2.57	3.13
FEV_1 - % predicted	84.0	32.0	135.0	74.64	84.51	95.27
FVC (litres)	3.4	1.0	6.2	2.71	3.34	4.09
FEV_1/FVC x 100%	75.7	35.0	99.0	71.5	77.0	81.5

Table 4.6. Summary of operative variables and outcomes (n = 745)

Variable	Yes (%)	Total (%)	Mean	Min	Max	Quartiles		
						25th	50th(Median)	75th
Length of operation (hrs)			2.0	0.5	14.5	1.0	1.5	2.5
Type of anesthetic:								
Local		15 (2.0)						
General		670 (89.9)						
Spinal		60 (8.1)						
*NG tube placement perioperatively	40 (5.8)							
Internal Medicine consultation perioperatively	54 (8.4)							
Duration of hospital stay (days)			4.3	1	70	1	3	6
Pulmonary complication	20 (2.7)							

*Out of a set of 690 where data on NG tube placement was available

Table 4.7. Frequencies of types of operations performed (n = 745)

Site	Frequency	%
Upper abdominal (above umbilicus)	70	9.4
Lower abdominal (umbilicus and below)	90	12.1
Laparoscopic intra-abdominal	78	10.5
Orthopedic (lower/upper limbs, back)	154	20.7
Arthroscopic orthopedic	3	0.4
Urologic	58	7.8
Neurosurgical	94	12.6
Other (eg., ENT, plastics, opthamologic)	198	26.6

Table 4.8. Pulmonary complications breakdown

Complication	Frequency	% (of 745)
Death	1	0.13
Respiratory failure requiring mechanical ventilation	2	0.27
Pneumonia	5	0.67
Atelectasis of lung or lobe requiring intervention	4	0.54
Pneumothorax or pleural effusion requiring intervention	1	0.13
Delayed weaning from assisted ventilation (≥48 hours after surgery)	7	0.94
Total:	20	2.68%

4.2. Bivariate Analysis

The bivariate associations between the preoperative/operative variables and postoperative pulmonary complications are outlined in Tables 4.9 – 4.11. Sensitivities and specificities of the variables after bivariate analyses, as well as odds ratios and their confidence intervals were calculated and are displayed in Table 4.12.

Table 4.9. Chi-square and Fisher's exact tests for significance of categorical variables and postoperative pulmonary complications

Variable		Pulmonary Complication Yes	Pulmonary Complication No	*p* Value
Smoking history:	Non-smoker	4	300	*0.062
	Ex-smoker	12	25	
	Current smoker	4	16	
History of URTI:	No URTI	17	61	*0.424
	URTI 2-4 weeks ago	0	45	
	URTI < 2 weeks ago	3	67	
History of COPD:	No COPD	17	694	*0.037
	Inactive COPD	1	19	
	Active COPD	2	12	
History of asthma:	No asthma	17	660	*0.324
	Inactive asthma	2	37	
	Active asthma	1	28	
Operative site:	Non-abdominal	10	575	0.002
	Lower abdominal	4	86	
	Upper abdominal	6	64	
Type of anesthetic:	General	18	652	*1.000
	Non-general	2	73	
Gender:	Male	11	348	0.537
	Female	9	377	
History of daily cough:	No cough	13	599	0.020
	Dry cough	2	70	
	Productive cough	5	56	
Exercise capacity:	< 1 flight of stairs or two blocks	3	72	*0.443
	≥ 1 flight of stairs or two blocks	17	653	
Cough test:	Positive	4	53	*0.059
	Negative	16	672	
Wheeze test:	Positive	0	26	*1.000
	Negative	20	699	
Forced expiratory time:	≥ 9 seconds	3	18	*0.016
	< 9 seconds	17	707	
Maximum laryngeal height:	≤ 4 centimetres	4	102	*0.511
	> 4 centimetres	16	623	
Wheeze on auscultation:	Positive	1	22	*0.470
	Negative	19	703	
Nasogastric tube placement perioperatively:	Yes	9	31	*0.000
	No	11	639	
Internal Medicine consultation preoperatively:	Yes	2	52	*0.668
	No	17	575	
If an ex-smoker, when did patient quit?:	> 12 months ago	10	218	*0.659
	6 - 12 months ago	0	11	
	2 - 6 months ago	1	16	
	< 2 months ago	1	13	

* Fisher's exact test used to determine *p* value

Table 4.10. Two-independent sample *t*-tests for significance of continuous variables and postoperative pulmonary complications

Variable	Pulmonary Complication (Mean ± SE) Yes	No	*p* Value
Age	70.25 ± 2.64	53.77 ± .61	*< 0.001
Height	169.75 ± 2.07	170.47 ± .36	0.742
Weight	75.35 ± 2.78	80.08 ± .71	0.272
BMI	26.15 ± .81	27.46 ± .22	0.323
If quit smoking < 2 months ago, # of weeks quit	2.00 ± --	.59 ± .50	*1.000
If smoked, total # of pack-years smoked	28.16 ± 4.55	19.20 ± .84	0.043
Total # pack-years smoked, including non-smokers	22.53 ± 4.45	16.29 ± .61	*0.005
FEV_1	1.97 ± .14	2.61 ± .03	< 0.001
FVC	3.08 ± .20	3.43 ± .04	0.111
FEV_1/FVC x 100%	64.65 ± 2.41	76.02 ± .33	< 0.001
Length of operation	3.63 ± .63	1.92 ± .06	*< 0.001

*Equality of variances not satisfied, therefore Mann-Whitney *U*-test used for *p* value calculation

Table 4.11 Chi-square and Fisher's exact tests for significance of newly dichotomized variables and postoperative pulmonary complications

Variable	Pulmonary Complication Yes	No	*p* Value
Ever smoked vs.	16	425	0.055
Never smoked	4	300	
URTI within last 4 weeks vs.	3	112	*1.000
No URTI	17	613	
Active and inactive COPD vs.	3	31	*0.058
No COPD	17	694	
Active and inactive asthma vs.	3	65	0.416
No asthma	17	660	
Operative site upper abdominal vs.	6	64	*0.007
Operative site non-upper abdominal	14	661	
History of daily cough vs.	7	126	*0.068
No history of cough	13	599	
Age ≥ 65 years vs.	16	210	< 0.001
Age < 65 years	4	515	
Smoked ≥ 40 pack years vs.	4	59	*0.080
Smoked < 40 pack years	16	666	
FEV_1 < 1 L/sec vs.	2	11	*0.045
FEV_1 ≥ 1 L /sec	18	714	
BMI ≥ 30 vs.	4	209	0.389
BMI < 30	16	516	
FVC < 1.5 L vs.	0	10	*1.000
FVC ≥ 1.5 L	20	715	
Length of operation ≥ 2.5 hours vs.	13	196	< 0.001
Length of operation < 2.5 hours	7	529	

*Fisher's exact test used to determine *p* value

Table 4.12. Fisher's exact test for significance of alternatively dichotomized variables and postoperative pulmonary complications

Variable	Pulmonary Complication		*p* Value
	Yes	No	
URTI < 2 weeks ago vs.	3	67	0.423
No URTI	17	658	
Active COPD vs.	2	12	0.051
No COPD	18	713	
Active asthma vs.	1	28	0.553
No asthma	19	697	
Operative site abdominal vs.	10	150	0.004
Non-abdominal	10	575	
Operative site lower abdominal vs.	4	86	0.288
Non-lower abdominal	16	639	
Operative site upper abdominal vs.	6	64	0.005
Non-abdominal	9	498	
History of productive cough vs.	5	56	0.019
No history of cough	15	669	

Table 4.13. Sensitivities, specificities, and odds ratios for all variables and postoperative pulmonary complications after bivariate analysis.

Variable	Sensitivity	Specificity	Odds Ratio (C.I.)
Age ≥ 65 years vs. Age < 65 years	0.80	0.71	9.81 (3.24, 29.64)
Smoked ≥ 40 pack-years vs. Smoked < 40 pack-years	0.20	0.92	2.82 (0.91, 8.71)
FEV_1 < 1 L/sec vs. FEV_1 ≥ 1 /sec	0.10	0.98	7.21 (1.49, 34.92)
BMI ≥ 30 vs. BMI < 30	0.20	0.71	0.62 (0.20, 1.87)
FVC < 1.5 L vs. FVC ≥ 1.5 L	0	0.99	—
Ever smoked vs. Never smoked	0.80	0.41	2.82 (0.94, 8.53)
URTI within last 4 weeks vs. No URTI	0.15	0.85	0.97 (0.28, 3.35)
Active and inactive COPD vs. No COPD	0.15	0.96	3.95 (1.10, 14.19)
Active and inactive asthma vs. No asthma	0.15	0.91	1.79 (0.51, 6.27)
Operative site upper abdominal vs. Operative site non-upper abdominal	0.30	0.91	4.43 (1.64, 11.92)
History of daily cough vs. No history of cough	0.35	0.83	2.56 (1.00, 6.55)
Length of operation ≥ 2.5 hours vs. Length of operation < 2.5 hours	0.65	0.73	5.01 (1.97, 12.75)
General anesthetic vs. Non-general anesthetic	0.90	0.10	1.08 (0.23, 4.43)
Male vs. Female	0.55	0.52	0.76 (0.31, 1.84)
Exercise capacity < 1 flight of stairs or two blocks vs. Exercise capacity ≥ I flight of stairs or two blocks	0.15	0.90	1.60 (0.46, 5.59)
Cough test positive vs. Cough test negative	0.20	0.93	3.17 (1.02, 9.82)
Wheeze test positive vs. Wheeze test negative	0	0.96	—
Forced expiratory time ≥ 9 seconds vs. Forced expiratory time < 9 seconds	0.15	0.98	6.93 (1.86, 25.77)
Maximum laryngeal height ≤ 4 centimetres vs. Maximum laryngeal height > 4 centimetres	0.20	0.86	1.53 (0.50, 4.66)
Positive wheeze on auscultation vs. Negative wheeze on auscultation	0.05	0.97	1.68 (0.22, 13.13)
Nasogastric tube placement perioperatively vs. No nasogastric tube placement perioperatively	0.45	0.88	16.87 (6.51, 43.69)
URTI < 2 weeks ago vs. No URTI	0.15	0.91	1.73 (0.50, 6.06)
Active COPD vs. No COPD	0.10	0.98	6.60 (1.38, 31.67)
Active asthma vs. No asthma	0.05	0.96	1.31 (0.17, 10.14)
Operative site abdominal vs. Non-abdominal	0.50	0.79	3.83 (1.57, 9.38)
Operative site lower abdominal vs. Non-lower abdominal	0.20	0.88	1.86 (0.61, 5.68)
Operative site upper abdominal vs. Non-abdominal	0.40	0.89	5.19 (1.79, 15.05)
History of productive cough vs. No history of cough	0.25	0.92	3.98 (1.40, 11.36)

4.3. Multivariate Analysis

Before the variables were selected to be included in the first step of the main effects model building they were examined for colinearity. It was recognized that including more than one spirometry variable would create the problem of colinearity, so the test FEV_1 was selected to be entered into the first step of the model because it is a favoured test in health care for assessing lung function and because it was statistically significant in the bivariate analysis.

Both "smoking" variables (ever smoked vs. never smoked, smoked $\geq$ 40 pack-years vs. smoked < 40 pack-years) also could not be entered into the first stage of model building so each was assessed in the model separately. Since "purposeful selection" was the method of choice for multivariate model building, all variables with p values of < .20 in the bivariate analysis and all variables thought to be clinically important were put into the multivariate model.

The variables chosen because of their significance ($p < .20$) in the bivariate analysis were: age $\geq$ 65 years vs. < 65 years, ever smoked vs. never smoked, $FEV_1 \geq 1$ L/sec vs. < 1 L/sec , length of operation $\geq$ 2.5 hours vs. < 2.5 hours, history of active COPD vs. no history of COPD, site of operation abdominal vs. non-abdominal, history of a daily productive cough vs. no history of cough, cough test, forced expiratory time, and NG tube placement. Four other variables, BMI $\geq$ 30 vs. < 30, general anesthetic vs. non-general anesthetic, gender, and maximum laryngeal height $\geq$ 4 cm vs. < 4 cm were added because they were thought of as clinically important, but were not significant in the bivariate analysis.

The model was fit and only two variables were found to be statistically significant at $p < .05$ using Wald's statistics. These variables were age $\geq$ 65 years, and NG tube placement perioperatively. A reduced model was fit and the likelihood ratio test was performed, comparing the initial and reduced models, to verify that the removed

variables were indeed insignificant. This was the case and the model remained at the two variables.

The assessment of confounding effects of variables that were removed was then done by observing for changes of > 20% in the regression coefficients (βs) of the other variables still in the model. Length of operation > 2.5 hours was found to be a confounder of NG tube placement because the change in the regression coefficient was 20.7%, and therefore was included in the final model.

While the model was built using all dichotomized variables, the model was also run using the continuous variables for age and length of operation. These variables were checked for linearity and, while the continuous variable for age was linear, the one for length of operation was not. Therefore, a newly categorized variable or the previously mentioned dichotomized length of operation variable would be fit in the final model. All clinically plausible interactions between the three variables in the model were fit into the multivariate model, one at a time, to identify, using Wald statistics, which ones were statistically significant at $p < .05$. None of the interactions was statistically significant. The final model, consisting of the variables age, NG tube, and length of operation, is shown in Table 4.14, with age and length of operation dichotomized.

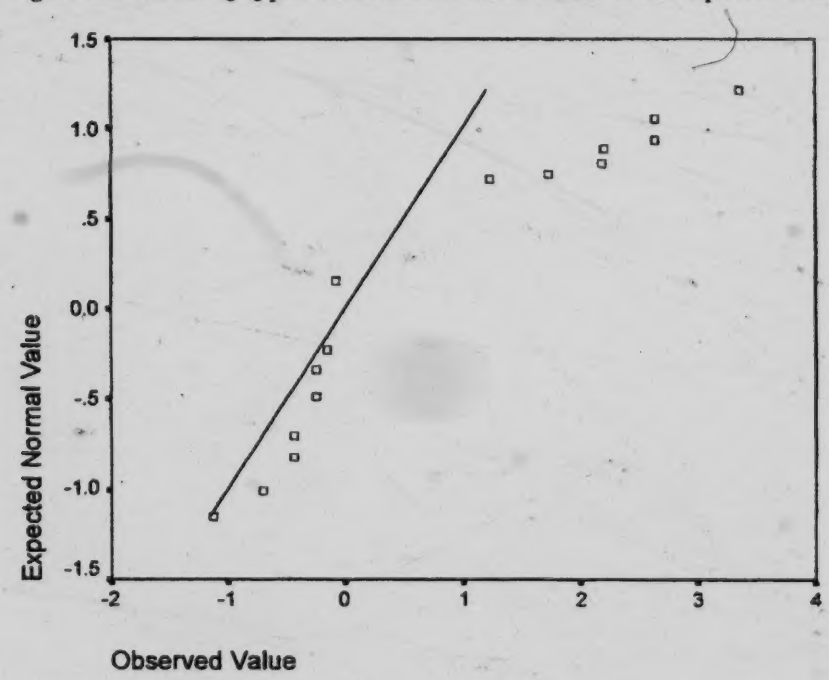
Table 4.14. Final model and parameter estimates after multivariate analysis

Variable	β	Std Error	Wald	df	Sig.	Exp (β)	95% C.Is for Exp (β)
Constant	-5.625	0.602	87.247	1	0.000	0.004	
NG tube	2.168	0.552	15.432	1	0.000	8.740	2.963, 25.77
Age ≥ 65 years	2.187	0.584	14.024	1	0.000	8.913	2.837, 28.04
Operation length ≥ 2.5 hours	1.141	0.534	4.564	1	0.033	3.131	1.099, 8.921

The Hosmer-Lemeshow test was not an appropriate test to determine the fit of this model because of the small number of outcomes (Hosmer & Lemeshow 2000). Therefore, the *p* value for the Hosmer-Lemeshow test statistic was invalid.

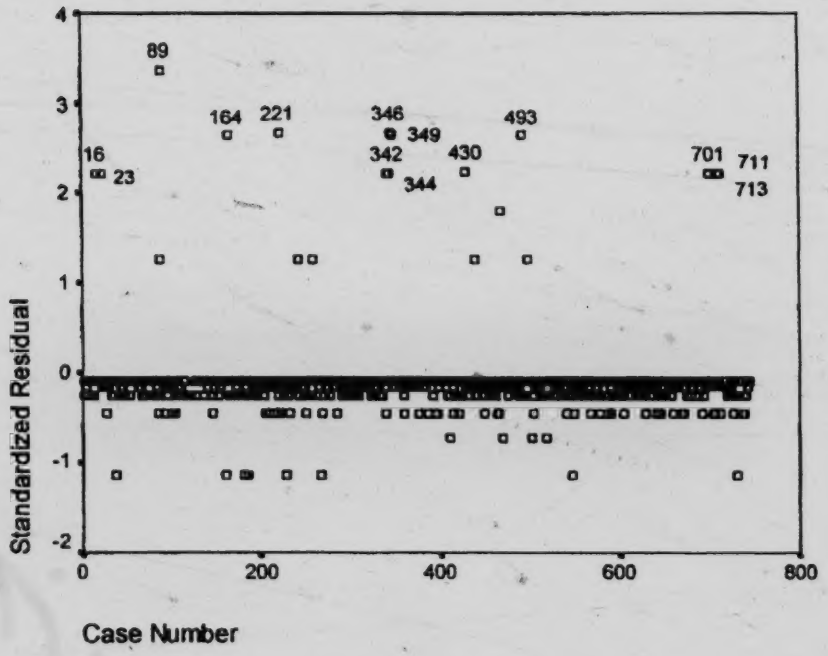
Since a single number summarizing the agreement of observed and fitted values could not be obtained, plotting diagnostics was useful to determine outliers. First, a normal probability plot of the deviances was observed (Figure 4.1.) The deviances do not appear to be normally distributed which means that there are cases for which the model does not fit well (SPSS 1999).

Figure 4.1. Normal Q-Q plot of deviances between observed and expected values



Second, a plot of the standardized residuals against the case sequence numbers was observed for large values or outliers beyond ± 2 standard deviations (Figure 4.2.) This plot revealed 14 outliers, all of which had a positive outcome of pulmonary complication.

Figure 4.2. Plot of standardized residuals with case identifications



The model does not appear to fit the data adequately and the results from this analysis should be interpreted with caution. Once the full data set is obtained (N=1,118), then methods for assessing the fit of the new model and diagnostics can be applied with greater confidence in obtaining a model for risk factor identification.

Chapter 5: Discussion

The results of the study reveal that certain preoperative and operative variables can be used to predict an increased risk for the development of pulmonary complications after nonthoracic surgeries. The three significant variables remaining after a multivariate analysis was performed (age, NG tube placement perioperatively, length of operation) have been cited in previous high quality studies as being significant indicators of pulmonary complications (Hall *et al.* 1996, Mitchell *et al.* 1998, Rao *et al.* 1992). While "age $\geq$ 60 years" was a significant factor in the preliminary study, the two other significant variables "smoking $\geq$ 40 pack years" and "maximum laryngeal height $\leq$ 4 cm" were not shown to be significant in this study. Thus, a focused physical examination preoperatively was proven to be more accurate in predicting postoperative pulmonary complications after nonthoracic surgeries in the preliminary study than in the present study. This was to be expected as the preliminary study participants were "high risk" patients being seen by internists. "Length of operation" was a significant variable in this study, but was not shown to be significant in the preliminary study.

Mitchell *et al.* (1982, 1998) included both "nasogastric intubation" and "site of operation" as possible risk factors for the development of lung complications after surgery. In both studies, nasogastric tube placement was found to be a more accurate indicator of risk than operative site in developing lung complications. The results of the present study are in agreement with the Mitchell *et al.* studies and show that the operative site loses significance after adjusting for perioperative nasogastric tube placement.

Prophylactic nasogastric intubation remains a common practice following gastrointestinal tract surgery. A review of some recently conducted prospective randomized trials, however, suggests that routine use of a nasogastric tube after abdominal surgery should be re-evaluated.

Savassi-Rocha *et al.* (1992) found a significantly higher incidence of atelectasis and pneumonia in patients with prophylactic nasogastric intubation following digestive tract surgeries than those without. A study conducted by Racette *et al.* (1987) demonstrates an increased incidence of atelectasis with the prolonged use of nasogastric suction compared with early nasogastric tube removal in the recovery room. Similarly, Donat *et al.* (1999) found that early nasogastric tube removal after urological surgeries, along with the use of the drug metoclopramide, reduced postoperative atelectasis. In another study where nasogastric tube placement was studied in conjunction with a drug, Cheadle *et al.* (1985) observed an increase in the number of complications of pneumonia in patients with a nasogastric tube compared to those without, regardless of whether the drug, cimetidine, was given or not. They concluded that prophylactic nasogastric decompression was unnecessary. Reasbeck *et al.* (1984) found that chest infections occurred noticeably more often in patients having nasogastric decompression after gastrointestinal surgeries compared with patients without nasogastric decompression. Even though this difference was not found to be statistically significant, the authors concluded that the routine use of nasogastric intubation after gastrointestinal resection is not warranted because there is significant discomfort and potential morbidity for the patient.

Other prospective randomized studies by Montgomer *et al.* (1996), Nathan and Pain (1991), Colvin *et al.* (1986), Wu *et al.* (1994), and Pearl *et al.* (1996), demonstrated that while the routine placement of nasogastric tubes postoperatively may not be statistically significant when observing for postoperative pulmonary complications, their use is not justified and should be reserved for highly selected circumstances or for patients developing complications.

Cheatham and colleagues (1995) conducted a meta-analysis of selected versus routine nasogastric decompression after elective laparotomy. They concluded that routine nasogastric decompression after these surgeries results in a significantly increased incidence of pulmonary complications and does not decrease the incidence of wound complications. Prophylactic gastric decompression was also found to be

associated with a delayed return of gastrointestinal tract function (Cheadle *et al.*, Pearl *et al.*) and an increased hospital stay (Cheadle *et al.*, Montgomery *et al.*, Wu *et al.*). Not to be ignored is the discomfort patients experience with nasogastric intubation. Cheadle and colleagues, and Pearl and colleagues reported subjective complaints of more ear pain, painful swallowing, and nasal soreness with nasogastric intubation than without, while Nathan and Pain also reported more complaints of nausea.

It is also important to note that the duration of hospital stay for the participants that developed pulmonary complications was significantly longer than for those with no pulmonary complications, with mean hospital stay sixteen days for those with pulmonary complications compared with three days for those without.

While this is the first large study using a blinded prospective cohort design to determine the predictive abilities of the history, physical examination, and operative factors for the development of lung complications after nonthoracic surgeries, there are still a number of limitations. The most obvious limitation of this study is the sample size. Even though this is the largest study of this type to date, the calculated sample size of 1,118 was not achieved for the present analysis. This resulted in a greater variability in the estimates of risk (wider confidence intervals) and thus a greater possibility of having "chance" as the explanation for the findings (Hennekens & Buring, 1987). Another limitation related to the smaller sample size than that needed is that the model was not validated in an independent data set. Since the study is continuing, this will occur after the analysis of the entire sample is obtained. Also, since the significant variable, NG tube placement, was not a variable under investigation in the preliminary study, the preliminary study data set was not used to validate the prediction model in this study.

There may also be limitations of this study related to the preoperative assessment. First, we relied on participant self-reporting to determine elements of their histories such as smoking. It is possible that participants may have underestimated their

smoking habit while in the presence of a health care provider. Second, the variable of "exercise capacity" may show inaccurate results because a number of the participants interviewed preoperatively were quite immobile and unable to walk moderate distances and/or climb stairs due to orthopedic problems precipitating their surgeries. Therefore, it was difficult to allocate a value for this variable in these circumstances because assumptions had to be made. Third, while great care was taken to reduce or eliminate bias entirely in this study, it is possible that investigator bias in determining preoperative variables was present. This type of bias would normally result in a stronger relationship between risk and outcome, however, since the only preoperative variable shown to be significant in this study after multivariate analyses is "age $\geq$ 60 years", bias is not likely a concern.

Finally, 32 participants did not have their charts available for both operative factors and outcome determination and, therefore, they could not be included in this study. These remaining participants were assumed to still be inpatients and may have possibly developed complications (including pulmonary) which could be the reason for their more lengthy stay in the hospital. As this study continues, these participants will eventually be included in the analyses of the larger, anticipated study group.

Chapter 6: Conclusions and Recommendations

The results of this study show that the development of pulmonary complications after surgical procedures is significantly associated with an increased length of hospitalization. It is important for the clinician to use available, accurate information to identify high risk patients and intervene where appropriate to prevent postoperative pulmonary complications in patients going for surgery. It would be useful for the clinician to have a clinical prediction rule to follow for evaluating preoperatively the patient's risk for developing lung complications after surgery. The results of this study indicate that the development of a clinical prediction rule for determining risk for postoperative pulmonary complications after non-thoracic surgeries is possible using elements of the preoperative assessment and operative factors. While the preliminary results of this study indicate the significance of two non-modifiable variables (age, length of operation), one variable, NG intubation perioperatively, is modifiable if done for the reason of prophylaxis. It is recommended that the prophylactic use of nasogastric intubation be questioned and possibly avoided. Other interventions for the prevention of pulmonary complications can be tested in high-risk people once further high-quality studies assessing pulmonary risk preoperatively is done. Finally, it is advised that the above clinical recommendations be applied only once the complete sample size is obtained, and the results provided here either confirmed or modified.

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Appendix A. Consent Form

CONSENT FORM

Part 1

Title of Project: Predicting Postoperative Pulmonary Complications After Non-Thoracic Surgeries: A Prospective Cohort Study

Principal Investigators:

Dr. Finlay McAlister	Division of General Internal Medicine, University of Alberta	407-1657
Kimberly Bertsch	Graduate Student, Public Health Sciences, University of Alberta	482-2154

Part 2 (to be completed by the research participant):

Do you understand that you have been asked to be in a research study?	Yes	No
Have you read and received a copy of the attached Information Sheet?	Yes	No
Do you understand the benefits and risks involved in taking part in this research study?	Yes	No
Have you had an opportunity to ask questions and discuss this study?	Yes	No
Do you understand that you are free to refuse to participate or withdraw from the study at any time? You do not have to give a reason and it will not affect your care.	Yes	No
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records?	Yes	No

This study was explained to me by: _____

I agree to take part in this study

_____	_____	_____
Signature of Research Participant	Date	Witness
_____		_____
Printed Name		Printed Name

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____	_____
Signature of Investigator or Designee	Date

The Information Sheet Must Be Attached To This Consent Form And A Copy Given To The Research Participant

Appendix B. Information Sheet

INFORMATION SHEET

Title of Project: Predicting Postoperative Pulmonary Complications After Non-Thoracic Surgeries: A Prospective Cohort Study

Principal Investigators:

Dr. Finlay McAlister	Division of General Internal Medicine, University of Alberta	407-1657
Kimberly Bertsch	Graduate student, Public Health Sciences, University of Alberta	482-2154

Purpose: To determine which parts of the medical history, physical examination, or routine tests done before an operation accurately predict who will, or will not, have lung problems after their operation.

Background: Although lung problems (like pneumonia or collapse of part of a lung) are the most common non-surgical complications after surgery, very little research has been done to determine how to predict which individuals are at high risk for these problems after their operation. In this study, we are collecting all the information that is normally collected during a preoperative medical consultation; thus, you will not be asked any questions or have any examinations or tests that wouldn't normally be done. If you decide to participate in this study, some of the information collected at this visit will be entered into a database with hundreds of other patients (your name, healthcare number, birth date, or anything that could identify you will not be put into the database to maintain confidentiality). We will then analyze this database to find out which questions, physical examination manoeuvers, or tests are most useful in predicting lung problems after an operation. By knowing this information, we can streamline our assessments of patients and more accurately identify individuals who are at high risk after their operation (and thus need closer attention and possibly treatment).

Procedures: As described above, if you decide to participate in this study, you will not be asked any questions or be subjected to any tests that we would not normally do as part of a complete medical assessment before an operation. Thus, involvement in this study will not require any extra time or effort for you than would normally be the case for a pre-surgery assessment.

Benefits: As nothing will be done in this study that is not part of the routine pre-surgery work-up, you are unlikely to gain any direct benefit from participation in the study. However, we believe that collecting the pre-surgery information on several hundred patients like yourself will allow us to figure out which parts of the assessment we routinely do are most useful in predicting risk of lung problems after an operation.

Risks: None (since nothing will be done in this study that is not part of the routine pre-surgery work-up).

Confidentiality: If you participate, your personal health information will not be shared with anyone other than your surgeon and family physician. Some of the information that we collect will be entered into a database of several hundred participants, but your name, birth date, healthcare number, or anything that could be used to identify you will not be entered to maintain confidentiality. You will not be identified in any presentations or publications of this study. Analysis of the aggregate data will be done by the study investigators listed above (again, without any linkage with data which could identify you).

Freedom to withdraw: You are free to withdraw from the study at any time. You do not have to give a reason, and it will not affect your care.

Additional contacts: If you have any concerns about any aspect of this study, you may contact the Patient Concerns Office of the Capital Health Authority at 407-1040. This office has no affiliation with any of the study investigators.

Appendix C. Participant Data Entry Form

PATIENT ENTRY FORM

Investigator ID: PREOP10002

Clinical Exam

1. HISTORY

Patient ID:

Are you the first contact physician for this patient?

☐ yes 1
☐ no 2

Patient age: (years old)

Height: (cm)

Weight: (kg)

Patient sex:
☐ female 1
☐ male 2

Smoking status:

Ever smoked:
☐ yes 1
☐ no 2

Still smoking:
☐ yes 1
☐ no 2

If 'No' to still smoking, indicate when patient quit:
☐ < 2 months ago 1
☐ 2-6 months ago 2
☐ 6-12 months ago 3
☐ > 12 months ago 4

If < 2 months ago, specify # of weeks since stopped:
(weeks)

Total # of pack/years:

Recent URTI (within 4 weeks of planned operation):

- ☐ yes 1
- ☐ no 2

If yes, was the URTI:

- ☐ < 2 weeks ago
- ☐ 2-4 weeks ago

Length of stay in hospital preop (only for inpatients):
(days)

Self-reported history of COPD (i.e. previously told they have emphysema, chronic bronchitis, or obstructive airways disease OR receiving bronchodilators chronically for COPD):

- ☐ yes 1
- ☐ no 2

If 'Yes' to hx of COPD, is it:

- ☐ currently active 1
- ☐ currently inactive 2

History of asthma (i.e. previously told they have asthma or reversible obstructive airways disease OR receiving bronchodilators or inhaled steroids chronically for asthma):

- ☐ yes 1
- ☐ no 2

If 'Yes' to hx of asthma, is it:

- ☐ currently active 1
- ☐ currently inactive 2

History of daily cough:

- ☐ yes 1
- ☐ no 2

If 'Yes' to daily cough, is it:

- ☐ dry 1
- ☐ productive 2

Exercise capacity (whichever is greater):

- ☐ < 1 flight of stairs or 2 blocks 1
- ☐ >= 1 flight of stairs or 2 blocks 2

2. PHYSICAL EXAMINATION

Cough test:
☐ +ve 1
☐ -ve 2

Wheeze test:
☐ +ve 1
☐ -ve 2

Forced expiratory time:
☐ < 9 seconds 1
☐ > = 9 seconds 2

Maximum laryngeal height:
☐ < = 4 cm 1
☐ > 4 cm 2

Wheezing on auscultation:
☐ +ve
☐ -ve

---

3. INVESTIGATIONS

a. Pre-op spirometry (MANDATORY)
FEV^1: (ml)
FVC: (ml)

---

b. Oxygen saturation on room air
(OPTIONAL – only if part of routine workup)
%

---

c. Arterial blood gases on room air
(OPTIONAL - only done if part of routine workup)
pH:
pCO^2: %
pO^2: %
HCO^3: %

---

d. Chest X-ray (OPTIONAL – only done if part of routine workup)
Normal CXR:
☐ yes
☐ no

If CXR not normal, please specify findings:

4. OPERATIVE FACTORS

The operation is:

- ☐ Elective 1
- ☐ urgent/emergent 2

Nasogastric tube placement perioperatively?

- ☐ Yes 1
- ☐ No 2

Site of operation:

- ☐ upper abdominal (above umbilicus) 1
- ☐ lower abdominal (umbilicus and below, including inguinal) 2
- ☐ laparoscopic intra-abdominal 3
- ☐ orthopedic (lower/upper limbs, back) 4
- ☐ arthroscopic orthopedic 5
- ☐ urologic (e.g. TURPs) 6
- ☐ neurosurgical (cerebral vx. Spinal) 7
- ☐ other (ENT, plastics, ophthalmologic) 8

Length of operation: (hours)

Type of anesthetic:

- ☐ local 1
- ☐ general 2
- ☐ spinal 3

Was there an Internal Medicine consultation pre-operatively?

- ☐ Yes 1
- ☐ No 2

REFERENCE STANDARD

Did the patient experience a clinically significant postoperative pulmonary complication prior to discharge or postoperative day 7 (whichever comes first)?

- ☐ yes 1
- ☐ no 2

If 'Yes' indicate the type of complication:

- ☐ death
  Cause of death:
- ☐ Respiratory failure requiring mechanical ventilation or BIBAP
- ☐ Pneumonia
  Was the pneumonia treated with antibiotics:
- ☐ yes
- ☐ no
- ☐ Atelectasis of lung or lobe requiring intervention
- ☐ Pneumothorax or pleural effusion requiring intervention
- ☐ Delayed weaning from assisted ventilation (i.e. > = 48 hours after surgery)

Length of hospital stay: (days)

Appendix D. Summary of acceptability and reproducibility criteria for spirometry (CPSA, 1998)

Acceptability Criteria	To be considered acceptable maneuvers must have:
Artifact Free	No cough or glottis closure during first second of exhalation No early termination or cutoff Variable effort No leaking No obstruction of the mouthpiece
Satisfactory Start-of-Test	Extrapolated volume < 5% of FVC or 0.15L whichever is greater Time-to-PEF <120 ms (optional)- Rapid rise to peak flow No hesitation at start of exhalation
Satisfactory End-to-Test	> 6sec exhalation and/or a plateau in the volume/time curve > 1second in duration; or Reasonable duration or a plateau in the volume/time curve; or If the subject cannot or should not continue
3 Acceptable Tests Performed	After 3 acceptable tests have been performed apply reproducibility criteria to each of them
Reproducibility Criteria	**At least 2 maneuvers must meet the reproducibility criteria:**
FVC acceptable	2 largest FVC must be within 0.2L of each other
FEV_1 acceptable	2 largest FEV_1 must be within 0.2L of each other
Reproducibility Criteria Met	If reproducibility criteria are met, the test session may be concluded.
Reproducibility Criteria Not Met	If reproducibility criteria are not met testing must continue until: They are met; or 8 tests have been performed with no signs of meeting the reproducibility criteria; or The subject cannot or should not continue. Save 3 best maneuvers at minimum.

Appendix E. Standard subject normal range – values and calculations

NAME			NAME		
AGE 33 years			AGE		
HEIGHT 148cm			HEIGHT		
Date	FVC (L)	FEV_1 (L)	Date	FVC (L)	FEV_1 (L)
Oct 22/01	3.85	3.25			
Oct 22/01	3.83	3.10			
Oct 23/01	4.00	3.17			
Oct 25/01	3.90	3.15			
Oct 27/01	3.93	3.32			
Oct 27/01	3.73	3.27			
Oct 28/01	3.78	3.30			
Nov 1/01	3.85	3.10			
Nov 2/01	3.90	3.15			
MEAN	3.86	3.20	MEAN		
SD	.0814	.0849	SD		
MEAN ±2 SD	3.69, 4.02	3.03, 3.37	MEAN ±2 SD		

Appendix F. Equipment checks using the standard subject

Standard Subject, Name:			Standard Subject, Name:		
	FVC (L)	FEV_1 (L)		FVC (L)	FEV_1 (L)
Expected Mean ±2 SD	3.86 ± .163	3.20 ± .170	Expected Mean ±2 SD		
DATE			DATE		
Nov 1/01	3.97	3.37	July 21/02	3.94	3.13
Nov 7/01	3.83	3.27	July 28/02	4.04	3.15
Nov 8/01	4.12	3.32			
Nov 15/01	4.07	3.27			
Nov 22/01	4.07	3.10			
Nov 29/01	4.07	3.10			
Dec 7/01	3.96	3.15			
Dec 16/01	3.94	3.15			
Jan. 7/02	3.90	3.05			
Jan 14/02	3.85	3.17			
Jan 24/02	3.99	3.22			
Feb 4/02	3.90	3.10			
Feb 17/02	3.99	3.15			
March 3/02	3.96	3.01			
March 24/02	3.87	3.03			
April 3/02	3.91	3.25			
April 10/02	3.87	3.15			
April 28/02	3.90	3.05			
May 8/02	4.04	3.32			
June 4/02	3.90	3.20			
June 17/02	3.94	3.25			
June 30/02	3.99	3.34			
July 8/02	4.04	3.29			
July 14/02	3.99	3.27			

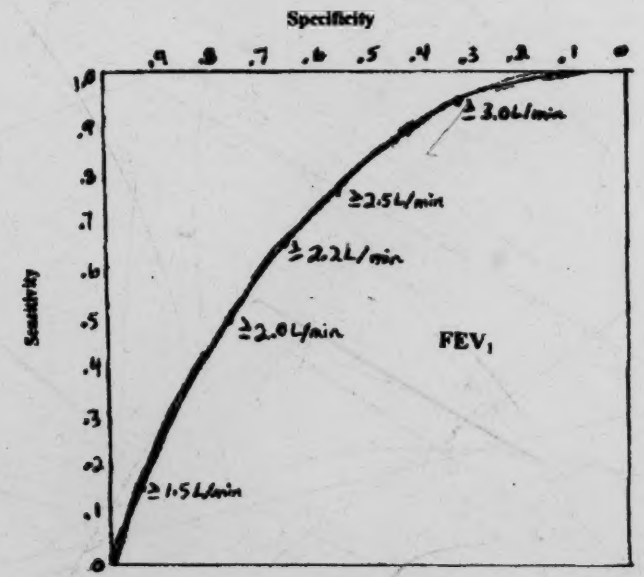
Appendix G. Examples of spirometry calibration (CPSA, 1998)

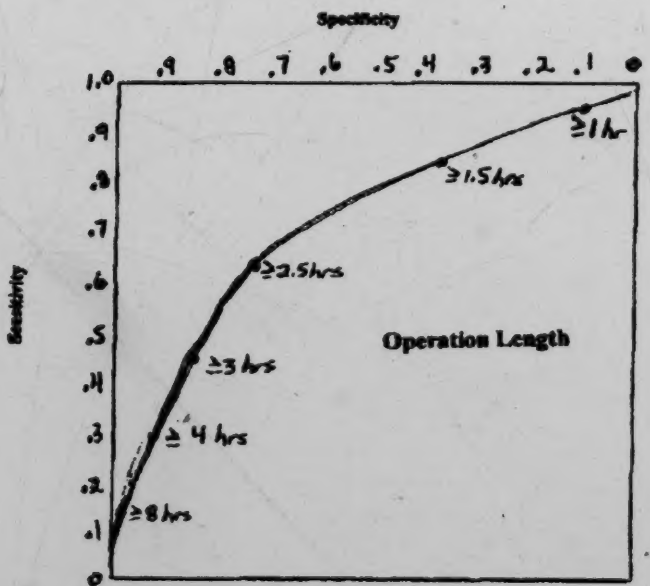
SYRINGE VOLUME = 3.00 L

DATE	FVC			DATE	FVC		
	Slow	Medium	Fast		Slow	Medium	Fast
Oct 16/01		2.98					
Oct 18/01		2.98					
Nov 7/01		3.00					
Nov 19/01		3.03					
Nov 23/01		3.00					
Dec 4/01		3.00					
Dec 13/01		3.05					
Dec 18/01		2.98					
Jan 8/02		2.98					
Jan 15/02		2.98					
Jan 23/02		2.98					
Jan 28/02		2.98					
Feb 3/02		3.00					
Feb 11/02		2.98					
Feb 24/02		3.08					
March 7/02		2.98					
April 7/02		3.03					
April 29/02		2.99					
June 10/02		3.03					
June 1/02		2.98					
July 3/02		2.98					
July 29/02		3.03					

1. Empty the calibration syringe into the machine using slow, medium and fast emptying rates.
2. Record the resultant FVC values for the three rates of emptying.
   - *Different speeds are necessary only for instruments making flow volume measurements.*
   - *If the results are outside 3% of the true value or if the rate of emptying causes values to vary by more than 3%, the machine must be serviced or replaced.*

Appendix H. Examples of sketches of receiver operator curves to determine cut-points for dichotomizing continuous variables





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kbertsch@telusplanet.net

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TABLES 1-2 – ACCURACY OF THE PREOPERATIVE ASSESSMENT IN PREDICTING PULMONARY RISK AFTER NONTHORACIC SURGERY.

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